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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/402,273	12/13/99	ULRICH J	9950-0002

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EXAMINER	
DIBRINO, M	
ART UNIT	**PAPER NUMBER**
1644	9

DATE MAILED: 07/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/402,273	Ulrich et al.
Examiner	**Art Unit**
Marianne DiBrino	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 10/1/99 and 6/4/01

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-3 and 6-14 is/are pending in the applica

4a) Of the above, claim(s) 3 and 9-14 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1, 2, and 6-8 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐disapproved.

12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No _____
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 10/1/99

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other.

DETAILED ACTION

1. Applicant's amendment filed 10/1/099 and Applicant's response filed 6/4/01 are acknowledged.

Applicant's said response has been entered.

Applicant's said amendment has been entered in part.

The direction (on page 2 of the said amendment) to change "has been" to --is-- on page 1 at line 23 of the instant specification has not been entered because the said phrase "has been" is not present at the specified location.

Claims 1-3 and 6-14 are pending.

2. Applicant's election with traverse of Group I (claims 1, 2 and 6-8), in Applicant's response filed 6/4/01 is acknowledged.

The basis for the traversal is that Applicant's assert that the pending claims are linked by a single inventive concept, and that the cited references do not render the claimed invention obvious. Applicant argues that the WO 92/16556 reference teaches a vaccine comprising HIV gp160 and 3-DMPL in the context of prophylactic and therapeutic treatment of HIV, but that the said reference does not teach or suggest that 3-DMPL can be used more widely as a general adjuvant in vaccine formulation. Applicant argues that there is nothing in the said reference that would lead one of [ordinary] skill in the art to believe that 3-DMPL is able to promote the preferential Th1 activity desired in allergen formulations, but not necessarily desired in vaccine formulations intended to treat and/or offer protection against infectious diseases such as HIV. The Applicant further argues that there would be no undue burden on the Examiner to examine all the claims together.

The Applicant's argument concerning that any reference teach or suggest that 3-DMPL is able to promote preferential Th1 activity desired in allergen formulations is moot because the instant claims, drawn to a product, do not recite that 3-DMPL is required to promote preferential Th1 activity, nor do the cited references teach that an adjuvant used in desensitization therapy must have the said activity. It is the Examiner's position that U.S. Patent No. 5,795,862, discussed at item #9 of this Office Action below, teaches a therapeutic composition for use in desensitization therapy comprising at least one allergen and further comprising an adjuvant and a carrier (especially claims 22 and 25, column 4 at lines 19-21 and 30-33, and the sentence spanning columns 7 and 8). Therefore, because claim 1 does not provide a special technical feature, the instant invention lacks an inventive step and therefore lacks Unity of Invention.

Regarding Applicant's comment about undue burden, the M.P.E.P. § 803 (July 1998) states that: "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The composition of Invention I (claims 1, 2 and 6-8) and the method of treatment of Invention II (3, 4 and 9-12) are classified in Class 424, subclasses 275.1, 278.1 and 283.1, whereas the method Invention III (claims 13 and 14) of preparing the composition of claim 1 is classified in Class 530, subclass 418. In addition, the method of Invention II involves a search of administration of allergen to a patient susceptible to allergy and the method of Invention III involves a search of methods for preparation of pharmaceutical compositions comprising use of cross-linking agents, precipitation and neutralization techniques and techniques for mixing allergen with tyrosine in strong acid.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 3, 4 and 9-12 (non-elected Invention II) and claims 13 and 14 (non-elected Invention III) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1, 2 and 6-8 are currently being examined.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: complete residence addresses lare not isted for inventors Ulrich and Worland.

4. Applicant is reminded of the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999; the following rejection is set forth herein.

Claims 1, 2 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir.

1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed pharmaceutical composition comprising an optionally modified allergen.

The instant claims encompass a pharmaceutical composition comprising an allergen that is modified in any way. There is insufficient disclosure in the specification on such a modified allergen.

The specification further discloses on page 1 at lines 30-32 that the present invention is a pharmaceutical composition comprising tyrosine, an optionally modified allergen and 3-DMPL. The specification discloses on page 2 at lines 15-16, that the allergen is optionally modified by reaction with a cross-linking agent such as dialdehyde, more particularly gluteraldehyde. The specification discloses on page 1 at lines 20-23 that the (tyrosine coprecipitated) allergen described in GB-A-1 377 074 and U.S. Patent No. 4,070,455 is modified by treatment with an agent such as gluteraldehyde which causes intra-molecular cross-linking and reduces the allergenicity of the product relative to the unmodified antigen. The specification discloses on page 2 at lines 9-11 that allergens may be derived from any allergy causing substance such as a pollen, food, insect venom, mould, animal fur or house dust mite. The specification further discloses on page 2 at lines 11-14 that an "allergen" includes a mixture of allergens which may be from a single source or more than one source, and also includes peptides containing one or more than one epitopes of an allergen such as allergen fragments.

An adequate written description of a "modified allergen" requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993).

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as "optionally modified allergen" without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of the allergen having been modified in some fashion. It does not specifically define any of the "modified allergens". It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by the said property of having been modified does not suffice to define the genus because it is only an indication of what the property the allergen has. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may

achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

The instant disclosure of an allergen modified by intra-molecular cross-linking to reduce allergenicity is not sufficient to describe the claimed genus which encompasses a large number of species. Because of this lack of disclosure of sufficient relevant identifying characteristics and because the genus is highly variant, the disclosure is insufficient to describe the claimed genus.

5. Claims 1, 2 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising an allergen modified by intra-molecular cross-linking to reduce allergenicity or comprising a polymerized allergen, does not reasonably provide enablement for making and/or using the claimed "optionally modified allergen". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification further discloses on page 1 at lines 30-32 that the present invention is a pharmaceutical composition comprising tyrosine, an optionally modified allergen and 3-DMPL. The specification discloses on page 2 at lines 15-16, that the allergen is optionally modified by reaction with a cross-linking agent such as dialdehyde, more particularly gluteraldehyde. The specification discloses on page 1 at lines 20-23 that the (tyrosine coprecipitated) allergen described in GB-A-1 377 074 and U.S. Patent No. 4,070,455 is modified by treatment with an agent such as gluteraldehyde which causes intra-molecular cross-linking and reduces the allergenicity of the product relative to the unmodified antigen. The specification discloses on page 2 at lines 9-11 that allergens may be derived from any allergy causing substance such as a pollen, food, insect venom, mould, animal fur or house dust mite. The specification further discloses on page 2 at lines 11-14 that an "allergen" includes a mixture of allergens which may be from a single source or more than one source, and also includes peptides containing one or more than one epitopes of an allergen such as allergen fragments.

The specification does not disclose the definition of "optionally modified" or of "modified". The specification does not disclose any modified allergens not of the type modified by treatment with an agent such as gluteraldehyde which causes intra-molecular cross-linking and reduces allergenicity.

There is no guidance in the specification as to what alterations result in a "modified allergen" and what degree of modification and allergenicity is acceptable. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions, additions, deletions would be acceptable to retain functional activity and what that degree of functional activity, i.e., allergenicity should be, especially as the fact that the relationship between the sequence of a peptide (allergen) and its tertiary structure (i.e., its activity) are not well understood and are therefore not predictable (Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction, Merz & LeGrand, Birkhauser Boston, pages 491-495, 1994, entire article, especially Section 6, paragraph 1, of record), it would require undue experimentation for one of skill in the art to arrive at other amino acid sequences that would have functional activity. In other words, since it would require undue experimentation to identify amino acid sequences that have functional activity, it would require undue experimentation to make and use the corresponding sequences. The enablement provided by the specification is not commensurate with the scope of the claims. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 2 and 6-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 2 and 6-8 are indefinite in the recitation of "the allergen". It is suggested that Applicant amend the said claims to recite "the said allergen.

b. Claims 2 and 6-8 are indefinite in the recitation of "the tyrosine". It is suggested that Applicant amend the said claims to recite "the said tyrosine".

c. Claim 1 is indefinite in the recitation of "optionally modified" because it is not clear what the metes and bounds of the said limitation are.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 2 and 6-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 96/34626 (IDS reference "AF") in view of WO 92/16556 (IDS REFERENCE "AE") and U.S. Patent No. 5,795,862.

WO 96/34626 teaches a pharmaceutical composition comprising tyrosine and an optionally modified allergen, i.e., a polymerized allergen (especially claims). WO 96/34626 teaches that the allergen is coated with and/or adsorbed onto tyrosine (especially page 1 at lines 17-18).

WO 96/34626 does not teach the said composition comprises 3-DMPL.

WO 92/16556 teaches a pharmaceutical composition comprising a modified or unmodified peptide antigen from HIV gp160 and 3-DMPL, and further teaches that 3-DMPL is an adjuvant and that adjuvants are useful to present immunogens effectively to the host immune system (especially claims, Abstract, page 8 at lines 20-34 and page 10 at lines 27-30).

U.S. Patent No. 5,795,862 discloses a therapeutic composition for use in desensitization therapy comprising at least one isolated flea saliva protein allergen and further comprising an adjuvant and a carrier (especially claims 22 and 25, column 4 at lines 19-21 and 30-33, and the sentence spanning columns 7 and 8).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included the 3-DMPL adjuvant of WO 92/16556 in the pharmaceutical composition taught by WO 96/34626 as for the therapeutic composition disclosed by U.S. Patent No. 5,795,862 comprising an allergen, an adjuvant and a carrier in order to make a pharmaceutical composition for desensitization therapy as disclosed by U.S. Patent No. 5,795,862.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 96/34626 teaches a pharmaceutical composition comprising tyrosine and an optionally modified allergen, WO 92/16556 teaches that adjuvants are useful to present immunogens effectively to the host immune system and that 3-DMPL is an adjuvant, and U.S. Patent No. 5,795,862 teaches a therapeutic composition for use in desensitization therapy comprising at least one allergen and further comprising an adjuvant and a carrier.

10. It is noted by the Examiner that there may be a spelling error in the instant application, i.e., "3-DMPL" is recited in the instant claims and disclosed in the instant specification, whereas WO 92/16556 teaches "3-D Mpl" (Abstract, for example) and U.S. Patent No. 4,912,094 discloses "d3-MPL" (column 9, line 63, for example).

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Marianne DiBrino

Marianne DiBrino, Ph.D.
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June 21, 2001

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